Towards *Staphylococcus epidermidis* biofilm dormancy characterization

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Despite being a common colonizer of human skin and mucosae, *Staphylococcus epidermidis* has a strong ability to adhere to medical devices surfaces. Therefore, *S. epidermidis* is among the most common causative agents of biofilm-associated infections. Dormant bacteria may be found among the metabolic heterogeneous cells within biofilms. These cells present a low metabolic activity and contribute to tolerance to the host immune response and antibiotics, and relapsing infections.

We performed an integrative analysis of dormancy within *S. epidermidis* biofilms, using an *in vitro* model previously described by our group [1]. We conducted a whole-transcriptome and proteome analysis of biofilms with higher number of dormant bacteria. Our data highlighted that: translation process was decreased in dormancy; transcripts involved in oxidation-reduction processes and proteins involved in catalytic activity and GTPase activity were up-regulated in dormancy; genes involved in the pyruvate metabolism were upregulated in dormancy. Additionally, in order to assess if dormant *S. epidermidis* biofilms influence the reactivity to host immune system, we carried on an immunoproteomic analysis by evaluating the immunoreactivity pattern to human sera. Interestingly, CodY protein was only reactive to sera in biofilms with higher number of dormant cells and ClpP protein only reactive when dormancy was prevented. Curiously, the ClpP deletion was previously associated with reduced ability to form *S. epidermidis* biofilms and with reduced virulence in a rat model of biofilm-associated infection [2]. These results may also suggest that magnesium is important to prevent nutrient limitation in *in vitro S. epidermidis* biofilms. Lastly, the clinical impact of dormancy among *S. epidermidis* isolates was studied. It was observed that both clinical and commensal isolates were able to develop a dormant state. In parallel, the effect of three different antibiotics against *S. epidermidis* biofilms with induced and prevented dormancy was assessed. Interestingly, our results point out to the development of a viable but-non culturable state within biofilms exposed to tetracycline and rifampicin, although rifampicin was also causing bacteria death.

Overall, using a multiple combined strategy, it was demonstrated that this dormancy model has a particular transcriptomic and proteomic profile, a distinct interplay with host and a relevant clinical impact.

References

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